=> d his

(FILE 'HOME' ENTERED AT 15:07:14 ON 26 AUG 2005)

FILE 'HCAPLUS' ENTERED AT 15:07:22 ON 26 AUG 2005

L1 1 US2005119219/PN OR (US2004-507472# OR WO2003-EP2538#)/AP,PRN

L2 1 IT2002-PD64#/AP, PRN

FILE 'REGISTRY' ENTERED AT 15:09:39 ON 26 AUG 2005

FILE 'HCAPLUS' ENTERED AT 15:10:03 ON 26 AUG 2005

L3 1 L1, L2

FILE 'REGISTRY' ENTERED AT 15:10:13 ON 26 AUG 2005

FILE 'HCAPLUS' ENTERED AT 15:10:13 ON 26 AUG 2005

L4 TRA L3 1- RN : 3 TERMS

FILE 'REGISTRY' ENTERED AT 15:10:15 ON 26 AUG 2005 L5 3 SEA L4

FILE 'WPIX' ENTERED AT 15:10:20 ON 26 AUG 2005 L6 1 L3

=> b hcap

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FILE COVERS 1907 - 26 Aug 2005 VOL 143 ISS 10 FILE LAST UPDATED: 25 Aug 2005 (20050825/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all 13 tot

L3 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:737790 HCAPLUS

DN 139:262427

ED Entered STN: 19 Sep 2003

TI Ester derivatives of hyaluronic acid, preparation, hydrogel materials by photocuring, and biomedical use

IN Bellini, Davide; Zanellato, Anna Maria

PA Fidia Advanced Biopolymers S.R.L., Italy

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C08B037-08

ICS C08J003-28; C08J003-075

CC 44-5 (Industrial Carbohydrates)

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Section cross-reference(s): 63
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     PATENT NO.
                                                                    DATE
                               DATE
                                            APPLICATION NO.
                         KIND
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                                20030918 WO 2003-EP2538
                                                                     20030312 <--
PΙ
     WO 2003076475
                         A1
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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                                           CA 2003-2478655
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     CA 2478655
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                                                                     20030312 <--
                          A1
     EP 1519962
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                 20050602 US 2003-507472
                                                                    20030312 <--
     US 2005119219
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                                 20020312 <--
PRAI IT 2002-PD64
                          A
                          W
                                 20030312 <--
     WO 2003-EP2538
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                        ______
                _ - - - -
 WO 2003076475 ICM
                        C08B037-08
                        C08J003-28; C08J003-075
                 ICS
                 ECLA A61L027/20+C08L5/08; A61L029/04D+C08L5/08;
 WO 2003076475
                        A61L031/04D+C08L5/08; C08B037/00P2F
                                                                               <---
 US 2005119219 NCL
                        514/054.000
OS
     MARPAT 139:262427
     The hyaluronic acid ester derivs., have carboxylic groups are partially
AB
     esterified with hydroxy groups of propiophenone derivs. Thus, 6.21 g
     tetrabutylammonium salt of hyaluronic acid, mol. weight 180,000 Da (10 meq.)
     are solubilized in 248 mL DMSO at room temperature, 2 g 2-hydroxy-4-(2-
     hydroxyethoxy)-2-methylpropiophenone (HHMP) bromide (7 meq.) are added,
     the solution is maintained at 37° for 48 h, 2.5% NaCl solution is added
     and the mixture is poured under stirring into 750 mL acetone, precipitating,
     filtering and washing three times with 100 mL acetone: water 5:1, three
     times with 100 mL acetone, and lastly vacuum-drying 24 h at 30°
     gave 5.3 g HHMP ester product.
     hyaluronic acid ester prepn photocuring hydrogel biol use
st
IT
     Drug delivery systems
        (controlled-release; hyaluronic acid esters photocured for hydrogels
        for)
TT
     Cell proliferation
        (fibroblast, scaffolds; hyaluronic acid esters photocured for hydrogels
        for)
IT
     Medical goods
        (hyaluronic acid esters photocured for hydrogels for)
IT
     Drug delivery systems
        (hydrogels; hyaluronic acid esters photocured for hydrogels for)
IT
     Fibroblast
        (proliferation, scaffolds; hyaluronic acid esters photocured for
        hydrogels for)
     124-22-1DP, Dodecylamine, amide with hyaluronic acid esters
IT
     601468-77-3DP, amide with dodecylamine 601468-77-3P, Hyaluronic acid
     2-hydroxy-4-(2-hydroxyethoxy)-2-methylpropiophenone ester sodium salt
     601468-78-4P
     RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (hyaluronic acid esters photocured for hydrogels)
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 6
RE
(1) Aeschlimann; WO 0016818 A 2000 HCAPLUS
```

- (2) Fidia Advanced Biopolymers Srl; WO 9637519 A 1996 HCAPLUS
- (3) Hercules Incorporated; EP 0749982 A 1996 HCAPLUS
- (4) Nguyen, K; BIOMATERIALS 2002, V23(22), P4307 HCAPLUS
- (5) Seikagaku Corporation; WO 9718244 A 1997 HCAPLUS
- (6) Waki; US 6031017 A 2000 HCAPLUS

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STRUCTURE FILE UPDATES: 24 AUG 2005 HIGHEST RN 861772-82-9 DICTIONARY FILE UPDATES: 24 AUG 2005 HIGHEST RN 861772-82-9

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y) /N:n

=> d ide 15 tot

- L5 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 601468-78-4 REGISTRY
- ED Entered STN: 09 Oct 2003
- CN Hyaluronic acid, ester with 2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-methyl-1-propanone, phenylmethyl ester, sodium salt (9CI) (CA INDEX NAME)
- MF C12 H16 O4 . x C7 H8 O . x Na . x Unspecified
- PCT Manual registration, Polyester, Polyester formed
- SR C
- LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 106797-53-9 CMF C12 H16 O4

CM 2

CRN 9004-61-9 CMF Unspecified CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM

CRN 100-51-6 CMF C7 H8 O

HO-CH2-Ph

1 REFERENCES IN FILE CA (1907 TO DATE) 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN L5

601468-77-3 REGISTRY RN

Entered STN: 09 Oct 2003 ED

Hyaluronic acid, ester with 2-hydroxy-1-[4-(2-hydroxyethoxy)phenyl]-2-CN methyl-1-propanone, sodium salt (9CI) (CA INDEX NAME) OTHER NAMES:

Hyaluronic acid 2-hydroxy-4-(2-hydroxyethoxy)-2-methylpropiophenone ester sodium salt

MF C12 H16 O4 . x Na . x Unspecified

Manual registration, Polyester, Polyester formed PCT

SR

LC STN Files: CA, CAPLUS, USPATFULL

> CM 1

CRN 106797-53-9 CMF C12 H16 O4

CM 2

CRN 9004-61-9 Unspecified CMF CCI PMS, MAN

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
                 1 REFERENCES IN FILE CA (1907 TO DATE)
                 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
                 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
     ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
L5
     124-22-1 REGISTRY
RN
ED
     Entered STN: 16 Nov 1984
     1-Dodecanamine (9CI) (CA INDEX NAME)
CN
OTHER CA INDEX NAMES:
    Dodecylamine (8CI)
OTHER NAMES:
     1-Aminododecane
     1-Dodecylamine
CN
CN
    Alamine 4
CN
    Amine BB
CN
    Armeen 12D
CN
     Farmin 20D
CN
     Kemamine P 690
    Lauramine
CN
CN
    Laurinamine
CN
    Laurylamine
     Monododecylamine
CN
CN
     Monolaurylamine
CN
     n-Dodecylamine
     n-Laurylamine
CN
     Nissan Amine BB
CN
     3D CONCORD
FS
DR
     126162-08-1, 27177-40-8
MF
     C12 H27 N
CI
     COM
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LC
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DETHERM*, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*,
        IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PIRA, PROMT,
       PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2,
       USPATFULL, VTB
          (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)
H_2N^- (CH<sub>2</sub>)<sub>11</sub>-Me
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
             4960 REFERENCES IN FILE CA (1907 TO DATE)
              744 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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4968 REFERENCES IN FILE CAPLUS (1907 TO DATE) 15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> b wpix;d all drn dcn 16 tot FILE 'WPIX' ENTERED AT 15:11:54 ON 26 AUG 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE LAST UPDATED: 23 AUG 2005 <20050823/UP> MOST RECENT DERWENT UPDATE: 200554 <200554/DW> DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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                                                                 <<<
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    GUIDES, PLEASE VISIT:
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    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
    FIRST VIEW - FILE WPIFV.
    FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<
>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
   PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/
    FOR DETAILS. <<<
'BIX BI, ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE
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L6
     2003-876823 [81]
                       WPIX
AN
DNC
    C2003-247398
     Ester derivatives of hyaluronic acid or hyaluronic acid derivatives, for
TI
    use as hydrogel material, comprising some carboxylic groups which are
     esterified with propiophenone derivatives.
DC
    A11 A96 B05 B07 D22
IN
     BELLINI, D; ZANELLATO, A M
     (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL; (BELL-I) BELLINI D; (ZANE-I)
     ZANELLATO A M
CYC
    104
PΙ
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           KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL
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    AU 2003227050
                    A1 20030922 (200431)
                                                      C08B037-08
                    A1 20050406 (200523) EN
                                                      C08B037-08
    EP 1519962
         R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
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    US 2005119219
                   A1 20050602 (200537)
                                                      A61K031-715
    WO 2003076475 A1 WO 2003-EP2538 20030312; AU 2003227050 A1 AU
ADT
     2003-227050 20030312; EP 1519962 A1 EP 2003-743875 20030312, WO
     2003-EP2538 20030312; US 2005119219 A1 WO 2003-EP2538
     20030312, US 2004-507472 20040910
FDT AU 2003227050 A1 Based on WO 2003076475; EP 1519962 A1 Based on WO
     2003076475
PRAI IT 2002-PD64
                          20020312
     ICM A61K031-715; C08B037-08
     ICS A01N043-04; C08J003-075; C08J003-28
AB
     WO2003076475 A UPAB: 20031216
    NOVELTY - Ester derivatives of hyaluronic acid or its derivatives,
     comprise some carboxylic groups which are esterified with propiophenone
     derivatives (I).
         DETAILED DESCRIPTION - Ester derivatives of hyaluronic acid or its
     derivatives, comprise some carboxylic groups which are esterified with
    propiophenone derivatives of formula (I).
          R = hydroxy, or 1-20C alkyloxy or heterocycle (both substituted by
    hydroxy group(s)); and
          R1-R3 = H, hydroxy, or 1-20C alkyl or 1-20C alkyloxy (optionally
     substituted with hydroxy group(s)).
          INDEPENDENT CLAIMS are also included for:
```

- (a) preparation of the ester derivatives, comprising reacting hyaluronic acid or its derivatives with the bromide of (I), where hydroxy group(s) of the substituent R is replaced by Bromine;
- (b) a hydrogel material consisting of a cross-linked product obtained by photocuring an ester derivative; and
- (c) a kit for implanting engineered cartilage by arthroscopic surgery, comprising an ester derivative dissolved in water or in an aqueous solution, a container for the ester derivative, and an endoscopic probe with optic fibers for the photocuring of the ester derivative.

USE - Useful in hydrogel material for biomedical materials, healthcare products, surgical articles consisting of catheters, guide channels, cardiac valves, vascular stents, soft tissue prostheses, prostheses of animal origin such as porcine heart valves, artificial tendons and organs, contact lens, and intra-ocular lenses, blood oxygenators, blood bags, surgical instruments, filtrations systems and laboratory instruments, for scaffolds for the growth of human and animal, pharmaceutical composition for topical, subcutaneous, intramuscular, intra-articular and intra-medullar administration, in the prevention of surgical adhesions, for the preparation of engineered connective tissues, engineered cartilage, viscoelastic substitutes of the nucleus pulpous of the intervertebral disk and visco-integrators of the vitreous humor (claimed).

ADVANTAGE - The hydrogel materials show valuable properties, and have absence of C=C unsaturation in the ester derivatives, without the addition of any component acting as catalyst for the cross-linking reaction and without any unsaturation within the molecule. The hydrogel materials also show sterility, excellent viscoelastic properties, compact, wall-to-wall type, three-dimensional structure, greater mechanical resistance, and have viscoelastic properties that vary according to how long they are exposed to irradiation, and to the type of aqueous solution used to obtain the hydrogel.

```
hydrogel.
     Dwg.0/1
FS
      CPI
      AB; GI; DCN
FA
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MC
            B04-L01; B04-N04; B06-H; B07-H; B10-E02; B10-E04; B10-F02; B12-M10;
            B14-E11; D09-C01
     0272-S; 0272-U; 0274-S; 0274-U; 0714-P; 0714-S; 0714-U; 1064-P; 1064-S;
      1064-U; 1706-S; 1706-U
         *01* DCN: R03231-K; R03231-T; R03231-Q; R03231-M; R03231-P; R06437-K;
          R06437-T; R06437-Q; R06437-M; R06437-P
*02* DCN: RA0121-K; RA0121-T; RA0121-Q; RA0121-M; RA0121-P
          *03* DCN: RA0019-K; RA0019-T; RA0019-Q; RA0019-M; RA0019-P
          *04* DCN: RA0120-K; RA0120-T; RA0120-Q; RA0120-M; RA0120-P
          *13* DCN: RA00H3-K; RA00H3-T; RA00H3-Q; RA00H3-M; RA00H3-P
          *14* DCN: RA00C8-K; RA00C8-T; RA00C8-Q; RA00C8-M; RA00C8-P
*15* DCN: RA00GC-K; RA00GC-T; RA00GC-Q; RA00GC-M; RA00GC-P
*05* DCN: RABXF5-K; RABXF5-T; RABXF5-Q; RABXF5-M; RABXF5-P
          *06* DCN: RABXF6-K; RABXF6-T; RABXF6-Q; RABXF6-M; RABXF6-P
     M2
          *07* DCN: RABXF7-K; RABXF7-T; RABXF7-Q; RABXF7-M; RABXF7-P
          *08* DCN: R03586-K; R03586-T; R03586-Q; R03586-M; R03586-P
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          *09* DCN: RA04KG-K; RA04KG-T; RA04KG-Q; RA04KG-M; RA04KG-P
*10* DCN: R00714-K; R00714-T; R00714-Q; R00714-M; R00714-P
      M2
           *11* DCN: R01064-K; R01064-T; R01064-Q; R01064-M; R01064-P
      M2
          *12* DCN: 0109-97801-K; 0109-97801-T; 0109-97801-Q; 0109-97801-M;
                       0109-97801-P
          *16* DCN: R00274-K; R00274-V; R00274-U
      M2
          *17* DCN: R01706-K; R01706-V; R01706-U
*18* DCN: R00272-K; R00272-V; R00272-U
      M2
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=> b home FILE 'HOME' ENTERED AT 15:12:00 ON 26 AUG 2005